

Based Upon: PCT/RU2004/000366

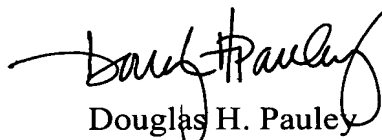
### REMARKS

Applicant respectfully requests entry of the above Preliminary Amendment to place this U.S. Patent Application in better form for examination and prosecution before the U.S. Patent and Trademark Office.

The claims have been amended to more definitely and fully claim the subject matter of Applicant's invention. Applicant urges that the above Preliminary Amendment introduces no new matter into this U.S. Patent Application.

Applicant sincerely believes that this U.S. Patent Application is now in condition for examination and prosecution before the U.S. Patent and Trademark Office.

Respectfully submitted,



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MAGNETICALLY OPERATED ASSAY METHOD FOR THE DETECTION THEREOF  
 [FERREED SORBENT. PREPARATION TECHNIQUE]

[SPHERE OF TECHNIQUE]

BACKGROUND OF THE INVENTION

Field of the Invention

[The inferred] <sup>This</sup> invention [pertains] <sup>relates</sup> to biology and medicine and might be applied for biological fluids purification and <sup>to</sup> <sup>a</sup> normalize condition of those to physiological standards.

[TECHNIQUE PRECEDING LEVEL] Discussion of Related Art

There is a known ferreed sorbent (FS), made of iron in the form of crystals, as taught by USSR Patent Reference with particle size of 10-15 nm [refer to e.g. certificate of authorship № 1589327, USSR, dated April 14<sup>th</sup>, 1988, IPC: C 01 G 49/08].

While exerting bactericidal effects, the known sorbent [however,] is limited in applicability, <sup>because</sup> as it can be used "in vitro" only.

The closest analogical prototype product is ferreed sorbent (FS), with the atomic centre <sup>or</sup> [core] as grading fraction with particle size of (0,1<sup>0.1</sup> - 1000) mc, made of iron, [or] iron oxides, [or] nickel, or iron-nickel alloy, and coated with <sup>a single</sup> [one] or double layer coat of carbon, [or] aluminum oxide, [or] silicium dioxide, [or] zirconium dioxide, [or] dextrane, e.g. sephadex, [or] gelatin, [or] albumin, [or] polysaccharide, e.g. amylum, <sup>or</sup> ion-exchange resins, e.g. cations or anions, where the coat upper layer is either conjugated with antibodies, or modified by pharmaceutical composition, e.g. antibiotics or phthalhydrazide salines, e.g. 5-amino-2,3-dihydro-1,4-dione salines, or else fermented e.g. with urease [refer to e.g.], such Russian Federation Patent [№] 2178313 [with priority date from] August 29<sup>th</sup>, 2000 [IPC: <sup>as taught by</sup> A61M1/16], dated

The above sorbent appears <sup>to be</sup> an effective remedy used for biological fluids extracorporeal restoration to physiological standards, providing clearance of e.g. blood from low-molecular, medium-molecular and high-molecular exotoxines and endotoxines with distraction of its rheological properties; <sup>correction of</sup> biological fluids enzymatic and immune constitution, as well as antiseptics of viruses and retroviruses pathogenic microflora. However, as such sorbent turns up a very expensive product, and a great quantity of the above sorbent is needed for <sup>having</sup> an appropriate course of treatment, and consequently the treatment is related with significant financial expenses.

<sup>taught by</sup> There is a known method of ferreed sorbent preparation technique <sup>(refer to</sup> e.g. <sup>Patant Reference dated</sup> USSR [certificate of authorship № 1589327, [with precedence date from] April 14<sup>th</sup>, 1988, IPC: C 01 G 49/08], including <sup>an</sup> iron powder volatilization procedure at low temperature ( $10^4 \times (0.3-5)^\circ \text{K}$ ) plasma in <sup>an</sup> argon atmosphere, and the derived volatile product is quenched and condensed in <sup>an</sup> argon gas flow <sup>and then</sup> the precipitated product in the form of crystals is transferred to <sup>a</sup> stabilizer containing dispersion medium, e.g. water at pH 7-9 or oil, and sustained there while being mixed, within (10-15) hours at the temperature (50-90) $^\circ \text{C}$  and at residual pressure of (1-3) MmHg <sup>[till]</sup> <sup>until</sup> the end of gas liberation.

The known method <sup>provides</sup> ensures the possibility to derivate sorbent in the form of iron particles (crystals) with particle size of (10-15) nm, however, due to small particle size the above sorbent has got low magnetic susceptibility values, consequently in order to withdraw sorbent out of the biological medium application of magnetic fields with intensity (1-3) tesla is required, which is unacceptable by medical norms <sup>(refer to, e.g.</sup>

specification to the <sup>such as taught by</sup> Russian Federation Patent [№ 2109522] <sup>[with precedence dated from]</sup>, dated August 1<sup>st</sup>, 1996, [IPC: A61M1/36].

[The closest <sup>One</sup> analogical prototype of ferreed sorbent preparation technique <sup>is taught by</sup> (refer to e.g.) Russian Federation Patent [№ 2109522] <sup>[with precedence dated from]</sup> August 1<sup>st</sup>, 1996, [IPC: A61M1/36], <sup>and includes</sup> [including] <sup>fractionating</sup> of high dispersed powder of Ferram reductum in inert gas flow with the velocity of <sup>0.02 to 1.00</sup> (0,02-1,00) m/s under exposure of <sup>an</sup> a magnetic field with <sup>the</sup> intensity of  $(10-10^3)$  A/u with subsequent thermal treatment of [the] received iron particles at the temperature of  $(1000-1500)^\circ$  C in inert gas flow containing coal and/or silicon oxide and/or aluminium oxide microparticles, after which treatment the ferreed sorbent particles surface are covered by biologically active compounds <sup>such as</sup> [food proteins or dextrane, or pharmaceutical preparations, or antibodies].

Such method <sup>ensures</sup> [ensures] <sup>a</sup> provides possibility to receive ferreed sorbent of certain chemical composition, effective at recession «in vivo» and «in vitro» of low, medium] and high molecular toxins, microflora and retroviruses. However, the above method is limited [in possibility of] <sup>to</sup> [receiving] [of] the ferreed sorbent with volumetrical particles, having predominantly proportionate dimensions with respect to both thickness of <sup>0.5-2.5</sup> (0,5-2,5) mcm and those particles surface dimensions corresponding to that form.

One object of the [INVENTION DISCLOSURE] <sup>SUMMARY OF THE INVENTION</sup> [The] “Ferreed Sorbent” invention <sup>is</sup> [based on the objective] to develop the sorbent similar in performance to analogous sorbent having substantially larger particles surface without any significant increase in weight of the sorbent core.

Another object of the  
 (The) "Ferreed Sorbent" invention [based on the objective] <sup>is</sup> to develop the procedure [providing the possibility] of receiving the sorbent with the core in a form of e.g. flake.

The above and other objects are  
 (The assigned task is) achieved [by enabling the fact that in] <sup>with</sup> the ferreed sorbent having a ferromagnetic core, with <sup>a single</sup> [one] or double layer coat or no coat, <sup>and</sup> [the core] [is] made in a form of a flake, with in-plane dimensions of (500-5000) mc, and thickness of <sup>0.1</sup> (0,1-1000) mc. Here the core is made either of iron, [or] nickel, [or] iron-nickel alloy, [or] iron or nickel alloy with titanium, [or] iron or nickel alloy with tantalum, [or] iron-nickel-titanium alloy, or iron-nickel-tantalum alloy.

Furthermore, the one layer coat is made either of carbon, [or] aluminum oxides, [or] silicon dioxide, [or] zirconium dioxide, [or] dextrane, e.g. from sephadex, [or] gelatin or albumin, [or] polysaccharide, e.g. amylum, or ion-exchange resins, e.g. cations or anions.

Here, in double layer coat the first closest to the core <sup>or inner</sup> [(inner)] layer is made either of carbon, [or] aluminum oxides, [or] silicon dioxide, [or] zirconium dioxide, and the second <sup>or outer</sup> [(outer)] layer of the coat is made either of dextrane, e.g. from sephadex, or gelatin or albumin, [or] polysaccharide, e.g. amylum, or ion-exchange resins, e.g. cations [or] anions.

<sup>Also,</sup> [Furthermore,] <sup>the</sup> the outer layer of the coat is either conjugated with antibodies, or modified by pharmaceutical composition, e.g. antibiotics or phthalhydrazide salines, e.g. 5-amino-2,3-dihydro-1,4-dione salines, or else fermented e.g. with urease.

The above and other objects are  
 [The assigned task is] achieved by [enabling] the fact that in <sup>the</sup> ferreed sorbent  
 generation method, [distinguishing by that] iron, [or/and] nickel, [or/and] titanium [or/and] and/or  
 tantalum powder is volatilized or fused in a low-temperature plasma with the  
 temperature of  $10^4 \times \{0,3-5\}^\circ\text{K}$ , and <sup>0.5</sup> [the] <sup>a</sup> received product of vaporous or fused particles  
 of respective metals or respective metals alloys is quenched and condensed in <sup>a</sup> gas  
 flow, e.g. <sup>an</sup> argon flow, and then the product settled as crystals or, correspondingly, as  
 microbars of respective metals alloys, is transferred to <sup>a</sup> disperse medium containing  
 stabilizer, e.g. water and/or oil, and while being mixed, sustained there within (5-15)  
 hours at the temperature  $(50-90)^\circ\text{C}$  and at residual pressure of (1-5) MmHg until gas  
 liberation ends <sup>Then,</sup> and after that <sup>a</sup> those crystals or microbars are treated by flattening e.g.  
 through pressing e.g. in a ball mill, until [getting] flakes <sup>are</sup> of the specified thickness, and  
 afterwards are repeatedly (up to 10 times) washed in distilled water, and then  
 separated from weak parts of flakes, treating with e.g. ultrasound of e.g. (200-300)  
 $\text{Vt/cm}^2$  capacity <sup>Then,</sup> and then <sup>are</sup> the received flakes <sup>a</sup> dried out e.g. in a hot air sterilizer at the  
 temperature of  $(80-110)^\circ\text{C}$ , and after that the dried flakes are fractionated in either  
<sup>an</sup> inert gas flow with the velocity of  $(0,02-1,00) \times \{0,02-1,00\} \text{ m/s}$  under exposure of magnetic field of  
 $5 \times (10-10^3) \text{ A/m}$  intensity, or <sup>by</sup> using e.g. centrifugation. Then, the specified size  
 sorbent cores with <sup>a</sup> layer-by-layer formed coat are extracted, and the received end  
 product is packed in light-protected and hermetically sealed containers and sterilized,  
 by e.g. U-rays, where sorbent received right after fractionating can be used as the end  
 product [as well]

Here, the first <sup>or inner</sup> (inner) layer of the coat is formed by thermal treatment of fractionated flakes at the temperature of (1000-1500)° C in <sup>an</sup> inert gas flow, e.g. <sup>a</sup> flow of argon, containing microparticles of either carbon, [or] silicon oxide, [or] aluminum oxide, or zirconium oxide.

Furthermore, the first layer of the coat is formed by blending with <sup>and</sup> using ultrasound exposure to fractionated flakes suspension within (1-10) minutes in heated to the temperature of (30-80)° C aqueous solution of dextrane, [or] gelatin or albumin, or amylum, with subsequent cooling of the above suspension down to the temperature of (4-10)° C, and the received precipitate is filled up with formalin, sustained there within (10-40) minutes, simultaneously being mixed, and after that dried out thoroughly at the temperature of (25-50)° C and grinded, then the received sorbent capsules, <sup>'</sup> (the end product) are filtered in <sup>a</sup> magnetic field.

Furthermore, the first layer of the coat is formed through adding an ion-exchange resin, e.g. amberlite into <sup>a</sup> fractionated flakes suspension in distilled water, heated up to the temperature of (40-60)° C, with subsequent cooling of the above suspension down to the temperature of (15-30)° C, with adding nitrous acid (HN<sub>2</sub>) diluted in water, sustaining within (10-15) minutes, cooling down to the temperature of (4-10)° C and elution of precipitate which is washed in <sup>a</sup> physiological solution <sup>and</sup> buffered in <sup>an</sup> aqueous solution of NH<sub>4</sub> OH foundation blend and NH<sub>4</sub> Cl salt.

Here, the second layer of the coat is formed by blending with using ultrasound exposure within (1-10) minutes to <sup>a</sup> suspension of ferromagnetics covered with carbon or silicon oxide, [or] aluminium oxide, [or] zirconium oxide coat in aqueous solution of [or] dextrane, [or] gelatin, [or] albumin, or amylum heated up to the temperature

(30-80)° C with subsequent cooling of the above suspension down to the temperature (4-10)° C, and the <sup>The</sup> received precipitate is filled up with formalin, sustained in there within (10-40) minutes <sup>of</sup> simultaneously being mixed, then dried out thoroughly at the temperature of (25-50)° C, grinded and the received sorbent capsules <sup>of</sup> the end product <sup>a</sup> are filtered in <sup>a</sup> magnetic field.

Furthermore, the second layer of the coat is formed through adding an ion-exchange resin, e.g. amberlite into <sup>a</sup> heated, up to the temperature of (40-60)° C, suspension of ferromagnetics, covered with carbon or silicon oxide, <sup>or</sup> aluminium oxide, or zirconium oxide coat, in distilled water, with <sup>a</sup> subsequent cooling of the above suspension down to the temperature of (15-30)° C, and adding and immixturing albumin, e.g. in the form of <sup>a</sup> serum, with subsequent adding of nitrous acid (HN0<sub>2</sub>) diluted in water, sustaining within (10-15) minutes, cooling down to the temperature of (4-10)° C and elution of precipitate which is activated by sustaining <sup>a</sup> within <sup>1.5</sup> (1, 2) hours in a modifier solution, then <sup>a</sup> washed in physiological solution <sup>a</sup> and buffered in aqueous solution of NH<sub>4</sub> OH foundation blend and NH<sub>4</sub> Cl salt.

Sodium periodate (NaIO<sub>4</sub>) or glutaric dialdehyde in (3-10)% solution of Na<sub>2</sub>SO<sub>4</sub> in water can be used here as a modifier.

Furthermore, while forming the outer layer of the coat, it is conjugated with antibodies by adding the ferreed sorbent with <sup>a single</sup> (one) or double layer coat into aqueous suspension; but it should be with the outer coat layer made of sephadex or albumin, modified e.g. with glutaric dialdehyde or sodium periodate, with serum, e.g. of blood, containing antibodies, specified to sorbed antigen, e.g. to systemic lupus erythematosus antigen, in buffered liquid with pH of <sup>6.5</sup> 6, 3-10, sustaining while being



mixed of the above compound within (1-3) hours at the temperature of (15-25)° C, subsequent<sup>to</sup> adding to the compound of sodium borhydrate, cooling down to the temperature of (4-10)° C,<sup>and</sup> repeated sustaining while being mixed within (1-3) hours, precipitate extraction and its buffering and drying out.

Furthermore, while forming the outer layer of the coat, it is modified with pharmaceutical composition through heating the ferreed sorbent suspension with <sup>a single</sup> (one) or double layer coat<sup>but</sup> with the outer coat made of e.g. dextrane or gelatin<sup>up</sup> to the temperature of (35-70)° C in physiological solution,<sup>and</sup> adding into <sup>it</sup> (there) a pharmaceutical composition in powder, e.g. antibiotic, e.g. oxaccillin, sustaining at thorough mixing at the above mentioned temperature within <sup>0.5-2.0</sup> (0,5-2,0) hours, <sup>a</sup> subsequent cooling of the <sup>a</sup> [above] compound down to the temperature of (4-10)° C, decanting of <sup>a</sup> supernatant fluid in <sup>a</sup> magnetic field,<sup>and</sup> washing the precipitate in running distilled water and its subsequent drying out.

Furthermore, while forming the outer layer of the coat, it is modified through preliminary dissolution of urease crystals in polyether, e.g. dibenzo-18 crown 6, immixture of the above solution with the suspension in distilled water of ferreed sorbent with the coat made of e.g. sephadex, sustaining while being mixed at the temperature of (25-40)° C within (2-5) hours and cooling down to the temperature of (4-10)° C, <sup>subsequently</sup> [subsequent] adding of formaldehyde and repeated sustaining within (1-3) hours,<sup>and</sup> draining out the supernatant fluid in the presence of <sup>a</sup> magnetic field and drying out the precipitate.

Furthermore, while forming the outer layer of the coat, it is modified through <sup>a</sup> heating up <sup>of an</sup> aqueous suspension of the ferreed sorbent with the coat made of e.g. dextrane, to the temperature of (40-70)° C, <sup>a</sup> subsequent immixture with zirconium saline powder, e.g. of respective phthalhydrazide saline, and (50-120) Vt/cm intensity ultrasound exposure to the above mixture within (1-10) minutes, <sup>a</sup> cooling <sup>of</sup> the received compound down to the temperature of (4-10)° C, <sup>and</sup> adding formaldehyde, sustaining while being mixed within (1-3) hours, <sup>and</sup> draining out the supernatant fluid in the presence of <sup>a</sup> magnetic field and drying out the precipitate.

DETAILED DESCRIPTION OF THE INVENTION  
[THE BEST VARIATION OF THE INVENTION EMBODIMENT]

Ferreed sorbent is made in the form of cores with <sup>a single</sup> [one] or double layer coat surrounding the core, <sup>'</sup> and with no coating.

To be used as cores for the ferreed sorbent [they take] powder is <sup>taken</sup> from ferromagnets, e.g. from iron (Fe), its oxides (Fe<sub>2</sub>O<sub>3</sub> or Fe<sub>3</sub>O<sub>4</sub> nickel (Ni), iron-nickel alloys, as well as from iron or nickel alloy with titanium (Ti), [or] from iron or nickel alloy with tantalum (Ta), from iron-nickel-titanium alloy, or from iron-nickel-tantalum-titanium alloy and the like magnetic sensible materials.

For the subsequent use fractions in the form <sup>of</sup> [or] flakes with the dimensions in plane of (500-5000) mc and with the thickness of (0,1-1000) mc are taken.

For getting cores for the ferreed sorbent, iron, [or/and] nickel,

<sup>and/or</sup>  
 [or/and] titanium, [or/and] <sup>and/or</sup> tantalum powder with particle size of  $(10^2-10^5)$  nm is  
<sup>and/or</sup> volatilized [or/and] fused in low-temperature plasma with the temperature of  
 $10^4 \times (0,3-5)^\circ\text{K}$ , and the received product volatilized <sup>and/or</sup> fused in the form of  
 respective metals or respective metals alloys with concentration of  $(0,1-0,5)$  <sup>0.1-0.5</sup>  
 volume % quenched down to the temperature of  $(50-80)^\circ\text{C}$  and condensed in a  
 reactor <sup>such as taught by</sup> (refer to e.g. description to <sup>Patent Reference</sup> USSR [certificate of authorship №] 1589327  
 [prioritized date from April 14<sup>th</sup>, 1988, IPC: C 01 G 49/08] in <sup>a</sup> gas flow, e.g. in an  
 argon flow, and then the product settled in the form of crystals or,  
 respectively, microbars of respective metals alloys, e.g. in the amount of  
 $(0,05-10)$  <sup>0.05</sup> mg, is transferred to the disperse medium containing stabilizer, e.g.  
 distilled water of  $(50-500)$  ml with pH of 7-9 and/or mineral, e.g. paraffin or  
 vegetable oil e.g. olive or sea-buckthorn oil, with preliminarily added e.g.  
 oleic acid in the amount of  $(2-20)$  volume %, and, while being mixed,  
 sustained in there within  $(5-15)$  hours at the temperature of  $(50-90)^\circ\text{C}$  and at  
 the residual pressure of  $(1-5)$  MmHg <sup>until</sup> [till] the end of gas liberation.

After that those crystals or microbars are treated by flatterring,  
 e.g. through pressing e.g. in a ball mill, <sup>until</sup> [till] having flakes of the specified  
 thickness, which then repeatedly (up to 10 times) are washed in distilled water,  
 and then weak flake parts are removed by exposing to ultrasound of e.g.  $(200-300)$  V<sub>T</sub>/sm<sup>2</sup> intensity in e.g. water.

The received material, <sup>or</sup> ~~(different size flakes and chip bits)~~ is dried in whole e.g. in a hot air sterilizer at the temperature of (80-110)°C, and then the dried product <sup>is</sup> ~~(flakes)~~ fractionated either in inert gas flow with velocity of ~~(0,02-1,00)~~ <sup>0.02-1.00</sup> m/c under the exposure of magnetic field with intensity of  $5 \times (10-10^3)$  A/M or by using centrifugation <sup>The</sup> ~~and the sorbent (flakes)~~ of the specified size is excreted in the form of cores, on which coats are formed layer by layer, and the acquired end product is packed up in lightproof hermetically closed containers and sterilized through e.g. U-rays; <sup>Here, the</sup> ~~here the~~ sorbent received right after fractionating can be chosen as the end product as well. The output of conditioned sorbent cores after fractionating makes (60-75) %.

For getting <sup>or</sup> ~~(forming)~~ of the first <sup>,</sup> ~~(closest to the core)~~ layer of the coat, the fractionated flakes are treated <sup>a</sup> ~~(at the temperature of (1000-1500)° C)~~ in <sup>a</sup> thermo oven in inert gas flow, e.g. in argon flow, containing microparticles of carbon (C), <sup>or</sup> ~~(silicon oxide (SiO<sub>2</sub>), (aluminum oxide (Al<sub>2</sub>O<sub>3</sub> or Al<sub>3</sub>O<sub>4</sub>), or zirconium oxide (ZrO<sub>2</sub>)).~~ <sup>A flow</sup> ~~(Flow)~~ velocity makes (0,02-1,2) m/s. Coating quality of cores depends on inert gas flow throughput rate, as well as on saturation of the gas with microparticles of coating material and the size of those particles. In the given examples, the thickness of the coat layer made with the above method makes (0,2-50) mc.

<sup>The</sup> ~~(Efficient)~~ output of <sup>is</sup> ~~(sorbent)~~ (70-85) %.  
The efficient

While forming [of] the first layer of the coat through covering sorbent cores with such substances like either dextrane, [or] gelatin, [or] albumin, or amylum, <sup>a</sup> fractionated flakes suspension in the amount of (2-20) g in (10-50) ml of distilled water is mixed with (50-100) ml of <sup>a</sup> heated to the temperature of (30-80)°C aqueous solution of either dextrane, [or] gelatin, [or] albumin, or amylum, with the blend ratio of (volume %): (50-95) % <sup>of the</sup> respective product, the rest is water; then <sup>is</sup> mixed within (1-10) minutes <sup>until</sup> [till] it gets homogeneous structure under the exposure of e.g. ultrasound dispergator "Y3ДH-2T" [refer to e.g. the description to the certificate of authorship № 1684616, [USSR]] <sup>such as taught by USSR Patent Reference</sup> and <sup>an</sup> ultrasound with <sup>an</sup> oscillation frequency (10-15) kHz and <sup>an</sup> intensity rate of (50-120) Wt/cm<sup>2</sup>; <sup>Then</sup> then the suspension is cooled e.g. in a refrigerator down to the temperature of (4-10)°C, then the precipitate received is filled up with formalin (aqueous solution HCHO), sustained in there within (10-40) minutes while simultaneously being mixed, <sup>and</sup> after that <sup>can</sup> [it should] be thoroughly dried up at the temperature of (25-50)° C, grinded and the received sorbent capsules, [the end product] <sup>are</sup> are filtered in magnetic field with the intensity of  $5 \times (10-10^3)$  A/m, of e.g. constant magnet made of samarium (8t)-cobalt (Co) alloy.

(0.5-3) <sup>A thickness</sup> [Thickness] of the coat layer made using the method above makes (0.5-3) mm.

<sup>The quantitative</sup> [Quantitative] output of sorbent makes (85-95) % out of <sup>the</sup> initial.

While forming [of] the first layer of the coat by using ion-exchange resin, e.g. (10-25) g of amberlite is added into <sup>the</sup> heated up to the

temperature of (40-60)° C fractionated flakes suspension of (2-5) g per (10-100) ml of distilled water, then the received compound is cooled down to the temperature of (15-30) ° C, <sup>then added is</sup> [add] nitrous acid (HNO<sub>3</sub>) diluted in water (in the amount of (1-10) vol. %), sustained within (10-15) minutes, then <sup>cooled</sup> [cool] again down to the temperature of (4-10)°C and then precipitate is excreted, which is washed in <sup>a</sup> physiological solution, <sup>and</sup> buffered <sup>until</sup> [till] it gets pH <sup>the</sup> [4,0±0,5] in aqueous solution of foundation of NH<sub>4</sub>OH or NH<sub>4</sub>Cl saline. 4.0±5.0

<sup>A thickness</sup> [Thickness] of the coat layer made by the above method makes <sup>0.2</sup> (0,2) mm.

<sup>The quantitative</sup> [Quantitative] output of sorbent makes (90-92) % out of <sup>the</sup> initial.

While forming [of] the second layer of the coat through covering the ferreed sorbent coated with either carbon or silicon oxide or aluminum oxide, or zirconium oxide with such substances like either dextrane, [or] gelatin, [or] albumin, or amylum, a suspension of ferromagnetics <sup>a</sup> [in the amount of (2-20) g per (10-50) ml of distilled water], covered with carbon, [or] silicon oxide, [or] aluminum oxide, or zirconium oxide coat, being mixed within (1-10) minutes under the exposure of ultrasound with intensity of (50-120) Vt/cm in (50-100) ml of heated to the temperature of (30-80)° C (50-95) % solution of dextrane, [or] gelatin, [or] albumin, or amylum in distilled water with <sup>a</sup> subsequent cooling to the above suspension down to the temperature (4-10)° C. The precipitate is filled up with formalin, sustained in there within (10-40) minutes while simultaneously being mixed and after that it is thoroughly dried out at

the temperature of (25-50)° C, grinded, and the acquired sorbent capsules or  
 (end product) are filtered in magnetic field with the intensity of  $5 \times (10-10^3)$   
 A/m.

*The thickness*  
 (Thickness) of the coat layer made by the above method makes  
 (0.5-3) [(0.5-3)] mm.  
*The quantitative*  
 (Quantitative) output of sorbent makes (85-95) % out of *the* initial.

While forming [of] the second layer of the coat by using ion-  
 exchange resin, a suspension of ferromagnetics, (in the amount of (0.2-0.5) g  
 per (10-100) ml of distilled water), covered with carbon, [or] silicon oxide, [or]  
 aluminum oxide, or zirconium oxide coat, heated up to the temperature of (40-  
 60)° C, then e.g (1-2) g of amberlite is added into there, and then the received  
 compound is cooled down to the temperature of (15-30) ° C, then *Then* nitrous acid  
 (HNO<sub>3</sub>) diluted in water, (in the amount of (1-10) vol. %) is added, sustained  
 within (10-15) minutes, then cooled again down to the temperature (4-10)° C  
 and the precipitate is excreted, which is activated by sustaining within [(1.5-2)] (1.5-2)  
 hours in a modifier solution, then washed in <sup>a</sup>physiological solution and  
 buffered [till] <sup>until</sup> it gets to pH [4.0±0.5] in aqueous solution of NH<sub>4</sub>OH foundation  
 and NH<sub>4</sub>Cl salt. Here, sodium periodate (NaIO<sub>4</sub>) or glutaric dialdehyde in <sup>a</sup>(3-  
 10)% solution of Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> in water can be used as <sup>a</sup>modifier.

*The thickness*  
 (Thickness) of the coat layer made by the above method makes  
 (0.2-1) [(0.2-1)] mm.  
*The quantitative*  
 (Quantitative) output of sorbent makes (90-95) % out of *the* initial.

Moreover, while forming the outer layer of the coat, it is conjugated with antibodies through adding serum e.g. of blood, into <sup>an</sup> aqueous suspension of ferreed sorbent with <sup>a single</sup> [one] or double coated, but with the outer coat made from sephadex or albumin, modified with e.g. glutaric dialdehyde or sodium periodate, <sup>in</sup> the amount of (1-50) ml of serum per (100-150) ml of suspension, containing antibodies specific to the antigen sorbed, e.g. to systemic lupus erythematosus antigen, in buffering liquid with pH of <sup>6.5</sup> 6.5-10, sustaining while the compound being mixed within (1-3) hours at the temperature of (15-25)° C, <sup>with</sup> subsequent adding of sodium borhydrate into the compound, cooling down to the temperature of (4-10)° C, repeated sustaining with simultaneous mixing within (1-3) hours, <sup>and the</sup> precipitate extraction and its buffering and drying out.

Here the respective coat layer thickness is increased for <sup>(0.2-0.5)</sup> (0,2-0,5) mm.

<sup>The quantitative</sup> [Quantitative] output of sorbent makes (92-95) % out of <sup>the</sup> initial.

Furthermore, while forming <sup>of</sup> the outer layer of the coat, it is modified with <sup>a</sup> pharmaceutical composition by heating up to the temperature of (35-70)° C of aqueous suspension of ferreed sorbent <sup>(10-20)</sup> (10-20) g of sorbent per (50) ml of distilled water <sup>a single</sup> with [one] or double layer coat, but the outer coat made of e.g. dextrane, or gelatin, in physiological solution <sup>0.9</sup> (0,9) % solution of NaCl in distilled water, <sup>and</sup> adding a pharmaceutical preparation powder, <sup>in</sup> the amount of (1-5) r per (10-50) ml of suspension, e.g. antibiotic, e.g. oxaccillin,



sustaining while simultaneous thorough mixing at the above mentioned temperature within  $\left[(0,5-2,5)\right]^{(0,5-2,5)}$  hours, subsequent cooling of the above compound down to the temperature of  $(4-10)^{\circ}\text{C}$ , decanting of the supernatant fluid in magnetic field with the intensity of  $5 \times (10-10^3)$  A/m, washing the precipitate in running distilled water and its subsequent drying out at the temperature of  $(25-40)^{\circ}\text{C}$ .

Here the respective coat layer thickness is increased for  $\left[(0,01-0,1)\right]^{(0,01-0,1)}$  mm.   
 [Quantitative] <sup>The quantitative</sup> output of sorbent makes  $(90-95)\%$  out of <sup>the</sup> initial.

Furthermore, while forming of the outer layer of the coat, it is modified by preliminary dilution of e.g.  $(1-5)$  g of urease crystals in  $(10-15)$  ml of polyether, e.g. of dibenzo-18 crown 6, blending the above solution with ferreed sorbent suspension in distilled water  $((10-15)$  hg of sorbent per  $(50-100)$  ml of water) with the coat made e.g. from sephadex-10, sustaining while mixed at the temperature of  $(25-40)^{\circ}\text{C}$  within  $(2-5)$  hours and cooling down to the temperature of  $(4-10)^{\circ}\text{C}$ , <sup>and</sup> subsequent adding of formaldehyde  $((25-30)$  ml per 100 ml of compound) and repeated sustaining while mixed within  $(1-3)$  hours, pouring out the supernatant fluid under the influence of magnetic field with the intensity of  $5 \times (10-10^3)$  A/m and precipitate drying out e.g. in a hot air sterilizer at the temperature of  $(50-85)^{\circ}\text{C}$ .

Here the respective coat layer thickness is increased for  $\left[(0,5-1)\right]^{(0,5-1)}$  mm.

*The quantitative*  
 [Quantitative] output of sorbent makes (90-95) % out of *the* initial.

Furthermore, while forming *[of]* the outer layer of the coat, it is modified through heating of aqueous suspension of ferreed sorbent with e.g. dextrane coat up ((15-20) g of sorbent per 75-100 ml of distilled water) to the temperature of (40-70)° C, *and* subsequent blending with zirconium saline powder of e.g. respective phthalhydrazide saline, e.g. 5-amino-2,3-dihydro-1,4-dion, and treating the above compound within (1-10) minutes with ultrasound of (15-25) kHz oscillation frequency and (50-120) Vt/cm<sup>2</sup> intensity, cooling of the received compound down to the temperature (4-10)° C, adding formaldehyde ((25-30) ml per 100 ml of compound), sustaining in there while mixing within (1-3) hours, *and* pouring out of supernatant fluid in the presence of magnetic field with the intensity of  $5 \times (10-10^3)$  A/m and precipitate drying out at the temperature of (25-45) C.

Here the respective coat layer thickness is increased for *0.01-0.1* mm.

*The quantitative*  
 [Quantitative] output of sorbent makes (90-95) % out of *the* initial.

#### INDUSTRIAL APPLICABILITY

Use of *a* ferreed sorbent having *a* substantially larger surface of the particles with no significant weight increase of its core, and the method of receiving such sorbent *provides* [allows to provide] effective cleaning of biological fluids, e.g. blood, out of low-, medium- and high-molecular exotoxines and endotoxines without disorder of its rheological properties, provide possibility

to correct ferment and immune structure of the biological fluids, as well as destruction of viruses and retroviruses pathogenic microflora while using appreciably low amount of the proposed ferreed sorbent, <sup>with respect to weight</sup> ~~[(with respect to weight)]~~ relatively to the amount of the analogous sorbent known earlier and specified for the same purposes.

Thus, in ~~the~~ <sup>takes</sup> view of the fact that biological fluid cleaning by using ferreed sorbent ~~(is taken)~~ <sup>takes</sup> place by interaction of its surface with the fluid being corrected, one can show that the effective particle surface of the known sorbent, <sup>a</sup> ~~(size of which in terms of length, width and thickness are on average commensurable at mass conservation, is significantly smaller than the surface of the proposed sorbent.~~

For example ~~(let's take)~~ <sup>consider</sup> a spherical particle.

Using known mathematical formulas, we ~~(will)~~ <sup>which</sup> get the following ~~(as sphere volume value (V<sub>sphere</sub>))~~ <sup>is</sup> equal to:  

$$V_{\text{sphere}} = 4\pi r^3/3$$
, where  $r$  ~~(is)~~ <sup>is</sup> sphere radius, and accordingly, the sphere surface area (S<sub>sphere</sub>) is equal to

$$S_{\text{sphere}} = 4\pi r^2, \text{ then}$$

$$S_{\text{sphere}} = 3 V_{\text{sphere}} / r$$

Considering that <sup>the</sup> particle mass is proportional to its volume, and assuming that after <sup>the</sup> above described procedure of acquiring sorbent particles in the form of flakes, a spherical sorbent particle will be reformed into <sup>a</sup> ~~(round)~~

flake/disk, <sup>. then</sup> then as the flake volume is  $V_{\text{flake}} = \pi R^2 \delta$ , and the surface area  $S_{\text{flake}} = \pi R^2$ , where  $R$  – flake radius, and  $\delta$  – its thickness, while  $\delta = 0,1$  g (in accordance with the abovesaid statement about some decrease of particle thickness), then [we have]  $S_{\text{flake}} = V_{\text{flake}} / 0,1$  g.

Considering that  $V_{\text{flake}} = V_{\text{sphere}}$ , then, as their masses are equal, we [will] get the following:

$$S_{\text{flake}} = 10 V_{\text{sphere}} / r$$

Taking into consideration that, there are two such surfaces on the flake, and putting the term (1) into the formula (2) we [will] get the following:

$$S_{\text{flake's full surface}} = 20 S_{\text{sphere}} / 3$$

The results received justify the above hypothesis that <sup>the</sup> in case of using [of] the sorbent being proposed, [the] each particle surface interacting with a biological fluid is significantly enlarged, and, consequently, consumption of sorbent and respective treatment costs are decreased.

Feasibility of effective application of the proposed ferreed sorbent extracted using the above-described methods is [testified] <sup>confirmed</sup> by the following examples:

Example 1. A non-pedigree dog weighing 12 kilos was injected (per os) 4,3 g of veronal. After 45 minutes amount of barbiturate in blood gets 118 mkg/ml.

Blood extracorporeal regeneration (correction) procedure was conducted using the expedient equipment (УКБЖ-1). The animal's blood was retrieved in portions of 10 ml, being then blended in equal volume proportions with ferreed sorbent suspension in physiological solution, which contained (mass. %): ferreed sorbent (core – nickel flake, coat inner layer - carbon, coat outer layer - dextrane) - 1,5; anticoagulant (heparin) -0,015; physiological solution as the balance; then the blood was sustained within 2-3 seconds and administered back into animal's organism.

About one liter of blood had been treated/processed during one session.

Indications before and after the correction session:

Creatinine (m mole/l)	1.45 [1,45]	(1,10)	1.10
Urea (m mole /l)	11.9 [11,9]	[6,2]	6.2
Bilirubin (total) (m mole /l)	25.0 [25,0]	[14,4]	14.4
Barbiturates (mkg/ml)	141.5 [141,5]	[14,2]	14.2

Furthermore, gastric lavage was made during the session, the animal was injected intravenously 500 ml of solution of electrolytes and 2 % glucose.

After the session, the animal was in the state of moderate severity, brisk reflexes.

The indications of sorbate effectiveness are shown in the following examples below, as well as effectiveness of selective and functional

properties of known ferreed sorbents, described, e.g. in the specifications [to the patent] of Russian Federation [№ 2178313 (refer to e.g. Russian Federation patent 2178313 with the priority dated from 29.08.2000, IASC: A 61 M 1/16)], and the results received during the researches with ferreed sorbent being proposed in <sup>this</sup> ~~the~~ present invention [hereby].

Example 2. 5 ml of carbofos solution was injected into the test-tube with 100 ml of a non-pedigree dog blood. Carbofos concentration in the blood was 0,015 mkg/ml.

The received blend was divided in two parts and each part was added 20 ml of ferreed sorbent suspension, where <sup>in</sup> ~~one~~ part was added the known ferreed sorbent suspension in physiological solution (cores as iron particles, coat layers as silicon oxide) in the amount of 1,0 g, while <sup>in</sup> ~~the~~ second part was added the proposed ferreed sorbent with the same material composition but with flake cores, in the amount of 0,012 g.

After mixing of the received compositions within <sup>1.5</sup> ~~1.3~~ minutes the supernatant fluid was decanted, and the precipitate was withhold using a magnet.

Carbofos concentration in the supernatant fluid received from the first blend made <sup>0.002</sup> ~~0.002~~ mkg/ml, and the supernatant fluid received from the second blend made <sup>0.012</sup> ~~0.012~~ mkg/ml.

Example 3. Into two different test-tubes each containing 20 ml of blood serum of a dog with simulated nephratonia (urea concentration in the

first test-tube was  $(26,4) \times 10^{-4}$  m mole/l, and  $(30,2) \times 10^{-2}$  m mole/l in the second), the following had been added: 200 mg of the known ferreed sorbent with the coating of sephadex-10 fermented with urease into the first test-tube; 30 mg of the ferreed sorbent being proposed with the cores in the form of titanium flakes with the coating analogous to the above specified, into the second test-tube.

After sustaining (while ~~shake~~ <sup>shaken</sup>) of the received compositions within 5 seconds and removal of the supernatant fluid in magnetic field, the urea content concentration in supernatant fluid in the first test-tube got  $(10,7) \times 10^{-7}$  m mole/l, and ~~it~~ got  $(12,1) \times 10^{-1}$  m mole/l in the second one.

Example 4. In two different test-tubes each containing 20 ml of phosphoric acid sodium saline solution ( $\text{NaH}_2\text{PO}_4$ ) in water the following had been added: 100 mg of the known ferreed sorbent with cation-modified (COON group polysaccharides) ion-exchange resin coating into the first test-tube; <sup>and</sup> 10 mg of the ferreed sorbent being proposed in the form of tantalum flakes with the coating analogous to the above specified - into the second test-tube.

After mixing (while ~~shake~~ <sup>shaken</sup>) of the received compositions and removal of the supernatant fluid in magnetic field, the concentration of phosphates in the supernatant fluid received from the first test-tube had reduced for 57 % comparatively to the initial, and the concentration of phosphates in the supernatant fluid from the second test-tube, correspondingly,

had reduced for almost half (for <sup>44.8</sup>44.8%) from the initial point of phosphates concentration.

Example 5. In two different test-tubes each containing 20 ml of sulphuric acid salines solution in water the following had been added: 100 mr of the known ferreed sorbent with anoinite-modified ( $\text{NH}_3$  x" group) ion-exchange resin coating into the first test-tube; <sup>and</sup> 20 mg of the ferreed sorbent being proposed in the form of iron-nickel flakes with the coating analogous to the above specified – into the second test-tube.

After mixing (while <sup>shaken</sup>shake) of the received compositions and removal of the supernatant fluid in magnetic field, the concentration of sulphuric acid salines in the supernatant fluids received from both of the test-tubes had reduced virtually for the same, i.e. for 72 % comparatively to the initial concentration in the first test-tube, and for <sup>73.4</sup>73.4% comparatively to the initial concentration – in the second test-tube.

Example 6. In two different test-tubes each containing 20 ml of blood of a patient with chronic renal-hepatic insufficiency disease the following had been added: 100 mg of the known ferreed sorbent with zirconium luminole saline-modified dextrane coating into the first test-tube; <sup>and</sup> 30 mg of the ferreed sorbent being proposed in the form of iron-titanium flakes with the coating analogous to the above-specified – into the second test-tube.

After mixing (while <sup>shaken</sup>shake) of the received compositions and



removal of the supernatant fluid in magnetic field, the concentration of phosphoric acid salines ( $\text{NaH}_2\text{PO}_4$ ) in the supernatant fluid received from the first test-tube had got  $\overset{0.07}{0.07}$  mg/ml; and the concentration of phosphoric acid salines ( $\text{NaH}_2\text{PO}_4$ ) in the supernatant fluid received from the second test-tube had got  $\overset{0.021}{0.021}$  mg/ml.  $\overset{0.61}{0.61}$  The initial concentration of the saline was  $\overset{0.61}{0.61}$  mg/ml.

Example 7. In two different test-tubes each containing 10 ml of blood serum of a patient with chronic renal-hepatic insufficiency disease the following had been added: 50 mg of the known ferreed sorbent with iron-nickel cores and urease-modified sephadex coating into the first test-tube; <sup>and</sup> 10 mg of the ferreed sorbent being proposed with iron-nickel cores with coating analogous to the above-specified – into the second test-tube.

After sustaining within 10 seconds and the supernatant fluid decanting (sorption) the urea concentration in the supernatant fluid received from the first test-tube had reduced for 23 % comparatively to the initial urea concentration in blood serum, and the urea concentration in the supernatant fluid received from the second test-tube had reduced for 35 % comparatively to the initial urea concentration <sup>the</sup> in blood serum.

Example 8. In two different test-tubes each containing 20 ml of blood serum of a patient with sepsis the following had been added: 150 mg of the known ferreed sorbent with iron-nickel cores and oxaccillin-modified gelatin coating into the first test-tube; <sup>and</sup> 15 mg of the ferreed sorbent being proposed with iron-nickel-titanium-tantalum alloy flake cores with coating

analogous to the above-specified – into the second test-tube.

After mixing while shaking of the test-tubes contents within 2 minutes, the supernatant fluid was decanted and the hard constituent was retained using a magnet field.

[ ]

Inoculation was made both on the patient's blood agar-agar and the blood having been exposed to ferreed sorbent (the supernatant fluids) from the both test-tubes.

Growth of streptococcus and staphylococcus colonies was observed in the inoculation of the patients' blood; <sup>and</sup> no such growth was observed in the inoculation of the blood taken from the test-tubes.

Example 9. In two different test-tubes each containing 10 ml of lymph plasma of a patient with sepsis the following had been added: 100 mg of the known ferreed sorbent with iron-nickel cores and dextrane coating into the first test-tube; <sup>and</sup> 15 mg of the ferreed sorbent being proposed with iron-nickel-titanium-tantalum alloy flake cores with coating analogous to the above-specified – into the second test-tube.

After mixing (while shaking) of the compositions received and removal of the supernatant fluid in magnetic field, inoculation was made both on the patient's lymph agar-agar and the lymph having been exposed to ferreed sorbent (the supernatant fluids) from the both test-tubes.

Growth of multiple staphylococcus colonies was observed in the

inoculation of the lymph with no lymph-separation; virtually no such growth was observed in the inoculation of the supernatant fluids taken from the test-tubes.

Example 10. In two different test-tubes each containing 5 ml of blood-tinted cerebrospinal fluid (a patient with craniocerebral injury) the following had been added: 50 mg of the known ferreed sorbent with iron cores and silicon oxide coating into the first test-tube; <sup>and</sup> 15 mg of the ferreed sorbent being proposed with iron-tantalum alloy flake cores with coating analogous to the above-specified – into the second test-tube.

After sedimentation the cerebrospinal fluid in the test-tubes had got light yellow <sup>color</sup> [colour].

Effectiveness of the developed preparation application is [testified in] <sup>confirmed by</sup> the experiments when doing the research on sorption capacity of the ferreed sorbent for each above-described variation for its performance, and at the same time the results <sup>are</sup> commensurable to the results of using analogous variations of the known ferreed sorbent were achieved at using significantly lower amounts of the ferreed sorbent being proposed.